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|-------------------------|-------------|----------------------|---------------------|------------------|
| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
| 09/456,306 | 12/08/1999 | NICOLE DUSCH | PM-265182 | 6287 |
| 909 | 7590 | 11/03/2004 | EXAMINER | |
| PILLSBURY WINTHROP, LLP | | | STEADMAN, DAVID J | |
| P.O. BOX 10500 | | | ART UNIT | PAPER NUMBER |
| MCLEAN, VA 22102 | | | 1652 | |

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 09/456,306 | DUSCH ET AL. | |
| | Examiner | Art Unit | |
| | David J Steadman | 1652 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 16 September 2004.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 35-41 and 43-52 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 35-38,40,41 and 43-52 is/are rejected.
 7) Claim(s) 39 is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
 Paper No(s)/Mail Date _____.
 4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____.
 5) Notice of Informal Patent Application (PTO-152)
 6) Other: Appendices A-D.

DETAILED ACTION

Status of the Application

- [1] Claims 35-41 and 43-52 are pending in the application.
- [2] Applicants' amendment to the claims, filed September 16, 2004, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.
- [3] Applicants' amendment to the specification, filed September 16, 2004, is acknowledged.
- [4] Receipt of an amended abstract to the specification, filed September 16, 2004, is acknowledged.
- [5] Receipt of a computer readable form of the sequence listing, a paper copy thereof, a statement of their sameness, and a statement that the paper copy of the sequence listing contains no new matter, all filed September 16, 2004, is acknowledged.
- [6] Applicants' arguments filed on September 16, 2004 have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [7] The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.
- [8] The indicated allowability of claims 35 and 37-41 is withdrawn in view of the new rejections as set forth below.

Claim Objections

[9] Claim 37 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 35 encompasses any nucleic acid that encodes SEQ ID NO:2, including all degenerate variants thereof. As such, claim 37 does not further limit claim 35.

Claim Rejections - 35 USC § 112, Second Paragraph

[10] Claim(s) 45-46 and 50-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 45 (claim 46 dependent therefrom) and 50 (claims 51-52 dependent therefrom) are confusing in that the claims recite "the nucleic acid molecule of claim 42," however, claim 42 has been canceled. It is suggested that applicants clarify the meaning of the claims. In the interest of advancing prosecution, the examiner has interpreted claims 45 and 50 as being dependent upon claim 44 instead of claim 42.

Claim Rejections - 35 USC § 112, First Paragraph

[11] Claims 36, 38, 40-41, and 50-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding SEQ ID NO:2, including SEQ ID NO:1, does not reasonably provide enablement for the

broad scope of claimed nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of polynucleotides of claims 36 (claims 38 and 40-41 dependent therefrom) and 50 (claims 51-52 dependent therefrom) for the reasons of record as set forth at item [9] of the Office action mailed June 16, 2004.

RESPONSE TO ARGUMENTS: Applicants argue the variants encompassed by the claims must retain the utility of the DNA sequence allegedly discovered by applicants. Applicants the specification enables a skilled artisan to make and use all variants encompassed within the scope of the claims using routine recombinant DNA techniques that are acknowledged by Example 14 of the Office's Revised Interim Written Description Guidelines Training Materials and pyruvate oxidase activity assays that were known in the art at the time of the invention. Applicants further argue the specification provides guidance as to the types of changes that are more likely to retain functionality. Applicants provide Attachments A and B as evidence. Applicants' argument is not found persuasive.

There is no dispute that recombinant DNA techniques for isolating and altering an encoding polynucleotide sequence and methods of assaying pyruvate oxidase enzymatic activity were known in the art at the time of the invention. It should be noted that, while the Office's Revised Interim Written Description Guidelines Training Materials

indicate that such techniques were known in the art, applicants are reminded that "the written description requirement is separate and distinct from the enablement requirement" (MPEP 2161). The fact that such techniques were known does not necessarily indicate an enabling disclosure for the scope of claimed polynucleotide variants. In this case, the specification is silent with regard to guidance for determining which of those nucleotides of SEQ ID NO:1 can be altered with an expectation of obtaining an encoded polypeptide having pyruvate oxidase activity. While it is acknowledged that the specification provides a general discussion of mutations (p. 10, lines 15-30), this disclosure fails to provide any specific guidance regarding altering the sequence of SEQ ID NO:1. The variants encompassed by claims 36 and 50 is vast, including any variant having an insertion, addition, deletion, or substitution and any combination thereof within the identity or hybridization limitation as recited in the claims. As the claims encompass any variant as described above and in view of the lack of guidance in the specification and prior art, at the time of the invention it was highly unpredictable as to which nucleotides of SEQ ID NO:1 could have been altered while encoding a polypeptide that maintains pyruvate oxidase activity as evidenced by state of the art as represented by Branden and Witkowski et al. (cited in a previous Office action), the teachings of which are undisputed by applicants. Because the claims encompass a vast number of variants, the specification provides no specific guidance regarding alteration of SEQ ID NO:1 with an expectation of obtaining the desired variant, there is a high level of unpredictability, and the experimentation required to

make all variants as broadly encompassed by the claims was not routine, undue experimentation is required to make all variants as encompassed by the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

[12] Claim(s) 35-38, 40-41, and 43-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Pompejus et al. (US Patent Application Publication 2004/0180408 A1).

The date relied upon for applying Pompejus et al. as prior art is August 31, 1999. The claims (in relevant part) are drawn to nucleic acids encoding SEQ ID NO:2, variants thereof, vectors and host cells, and a fragment of SEQ ID NO:1.

Pompejus et al. teaches a nucleic acid, SEQ ID NO:85, encoding a polypeptide that is 100% identical to SEQ ID NO:2 of the instant application (see Appendix A) and teach fragments and complements of their nucleic acid (p. 11). Pompejus et al. teach a vector comprising their nucleic acid and a host cell comprising said vector (pp. 14-17).

This anticipates claims 35-38, 40-41, and 43-52 as written.

[13] It should be noted that the polynucleotide of SEQ ID NO:1 of the instant application appears to be novel over Pompejus et al. While nucleotides 227 to 2086 of SEQ ID NO:1 are identical to the full length of SEQ ID NO:85 of Pompejus et al., nucleotides 1-226 of SEQ ID NO:1 are not disclosed by Pompejus et al. Thus, Pompejus et al. does not disclose the full length of SEQ ID NO:1 of the instant application. See Appendix B.

[14] It should also be noted that claim 39 has not been rejected as being anticipated or made obvious by Pompejus et al. According to the specification (see p. 18, middle), vector pCR2.1poxBint has a fragment of nucleotides 705 to 1579 of SEQ ID NO:1 (see Appendix C), encoding amino acids 127 to 417 of SEQ ID NO:2 (see Appendix D). The examiner can find no teaching in the prior art of record for a pCR2.1 vector having an insert of nucleotides 705 to 1579 of SEQ ID NO:1.

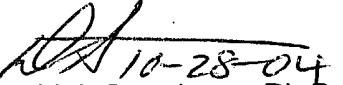
Conclusion

[15] Status of the claims:

- Claims 35-41 and 43-52 are pending.
- Claims 35-38, 40-41, and 43-52 are rejected.
- Claim 39 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:30 am to 4:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.


10-28-04
David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1652

Art Unit: 1652

APPENDIX ARESULT 1
us-10-781-014-85

Alignment Scores:

| | | | |
|------------------------|---------|---------------|------|
| Pred. No.: | 0 | Length: | 1860 |
| Score: | 2985.00 | Matches: | 579 |
| Percent Similarity: | 100.00% | Conservative: | 0 |
| Best Local Similarity: | 100.00% | Mismatches: | 0 |
| Query Match: | 100.00% | Indels: | 0 |
| DB: | 1 | Gaps: | 0 |

US-09-456-306-2 (1-579) x us-10-781-014-85 (1-1860)

| | | | |
|----|-----|---|-----|
| Qy | 1 | Met Ala His Ser Tyr Ala Glu Gln Leu Ile Asp Thr Leu Glu Ala Gln Gly Val Lys Arg | 20 |
| Db | 101 | ATGGCACACAGCTACGCAGAACATTAAATTGACACTTGGAAAGCTCAAGGTGTGAAGCGA | 160 |
| Qy | 21 | Ile Tyr Gly Leu Val Gly Asp Ser Leu Asn Pro Ile Val Asp Ala Val Arg Gln Ser Asp | 40 |
| Db | 161 | ATTTATGGTTGGTGGGTGACAGCCTTAATCGATGTGGATGCTGTCCGCCAATCAGAT | 220 |
| Qy | 41 | Ile Glu Trp Val His Val Arg Asn Glu Ala Ala Ala Phe Ala Ala Gly Ala Glu Ser | 60 |
| Db | 221 | ATTGAGTGGGTGACGTTGAAATGAGGAAGCGCGGGCTTGCAGCCGGTGCAGGAATCG | 280 |
| Qy | 61 | Leu Ile Thr Gly Glu Leu Ala Val Cys Ala Ala Ser Cys Gly Pro Gly Asn Thr His Leu | 80 |
| Db | 281 | TTGATCACTGGGAGCTGGCAGTATGTGCTGCTTCTGGTGCCTGGAAACACACACCTG | 340 |
| Qy | 81 | Ile Gln Gly Leu Tyr Asp Ser His Arg Asn Gly Ala Lys Val Leu Ala Ile Ala Ser His | 100 |
| Db | 341 | ATTCAGGGCTTTATGATTGCGATCGAAATGGTGCAGGGTGTGGCCATCGCTAGCCAT | 400 |
| Qy | 101 | Ile Pro Ser Ala Gln Ile Gly Ser Thr Phe Phe Cln Glu Thr His Pro Glu Ile Leu Phe | 120 |
| Db | 401 | ATTCCGAGTGCCAGATTGGTTCGACGTTCCAGGAAACGCATCCGGAGATTGTT | 460 |
| Qy | 121 | Lys Glu Cys Ser Gly Tyr Cys Glu Met Val Asn Gly Gly Glu Gln Gly Glu Arg Ile Leu | 140 |
| Db | 461 | AAGGAATGCTCTGGTACTGCGAGATGGTGAATGGTGGTGAGCAGGGTGAACGCATTG | 520 |
| Qy | 141 | His His Ala Ile Gln Ser Thr Met Ala Gly Lys Gly Val Ser Val Val Ile Pro Gly | 160 |
| Db | 521 | CATCACGCGATTCCAGTCACCATGGCGGTAAAGGTGTGGTAGTGATTCTGGT | 580 |
| Qy | 161 | Asp Ile Ala Lys Glu Asp Ala Gly Asp Gly Thr Tyr Ser Asn Ser Thr Ile Ser Ser Gly | 180 |
| Db | 581 | GATATCGCTAAGGAAGACGCGAGGTGACGGTACTTATTCCAATTCCACTATTCTGGC | 640 |
| Qy | 181 | Thr Pro Val Val Phe Pro Asp Pro Thr Glu Ala Ala Ala Leu Val Glu Ala Ile Asn Asn | 200 |
| Db | 641 | ACTCCTGTGGTGTCCCGGATCCTACTGAGGCTGCGCGCTGGTGGAGGCGATTAAACAAAC | 700 |
| Qy | 201 | Ala Lys Ser Val Thr Leu Phe Cys Gly Ala Gly Val Lys Asn Ala Arg Ala Gln Val Leu | 220 |
| Db | 701 | GCTAAGTCTGTCACTTGTCTGCGGTGCGGGCGTGAAGAATGCTCGCGCAGGTGTTG | 760 |
| Qy | 221 | Glu Leu Ala Glu Lys Ile Lys Ser Pro Ile Gly His Ala Leu Gly Gly Lys Gln Tyr Ile | 240 |
| Db | 761 | GAGTTGGCGGAGAAGATTAAATCACCGATCGGGCATCGCCTGGGTGTTACGGCGCTCGTG | 820 |
| Qy | 241 | Gln His Glu Asn Pro Phe Glu Val Gly Met Ser Gly Leu Leu Gly Tyr Gly Ala Cys Val | 260 |
| Db | 821 | CAGCATGAGAATCCGTTTGAGGTCGGCATGTCTGGCCTGCTGGTTACGGCGCTCGTG | 880 |
| Qy | 261 | Asp Ala Ser Asn Glu Ala Asp Leu Ile Leu Leu Gly Thr Asp Phe Pro Tyr Ser Asp | 280 |

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| | | | |
|----|------|---|------|
| Db | 881 | GATCGCGTCCAATGAGGC GGATCTGCTGATTCTATTGGGTACGGATTCCCTTATTCTGAT | 940 |
| Qy | 281 | PheLeuProLysAspAsnValAlaGlnValAspIleAsnGlyAlaHisIleGlyArgArg | 300 |
| Db | 941 | TTCCTTCCTAAAGACAACGTTGCCAGGTGGATATCAACGGTGCACATTGGTCGACGT | 1000 |
| Qy | 301 | ThrThrValLysTyrProValThrGlyAspValAlaAlaThrIleGluAsnIleLeuPro | 320 |
| Db | 1001 | ACCA CGGTGAAGTATCCGGTGACCGGTGATGTTGCTGCAACAATCGAAAATATTTCGCCT | 1060 |
| Qy | 321 | HisValLysGluLysThrAspArgSerPheLeuAspArgMetLeuLysAlaHisGluArg | 340 |
| Db | 1061 | CATGTGAAGGAAAAAACAGATCGTTCCCTCCTTGATCGGATGCTCAAGGCACACGAGCGT | 1120 |
| Qy | 341 | LysLeuSerSerValValGluThrTyrThrHisAsnValGluLysHisValProIleHis | 360 |
| Db | 1121 | AAGTTGAGCTCGTGGTAGAGACGTACACACATAACGTCGAGAAGCATGTGCCTATTAC | 1180 |
| Qy | 361 | ProGluTyrValAlaSerIleLeuAsnGluLeuAlaAspLysAspAlaValPheThrVal | 380 |
| Db | 1181 | CCTGAATACGTTGCCCTCATTTGAAACGAGCTGGCGGATAAGGATGCGGTGTTACTGTG | 1240 |
| Qy | 381 | AspThrGlyMetCysAsnValTrpHisAlaArgTyrIleGluAsnProGluGlyThrArg | 400 |
| Db | 1241 | GATAACCGGCATGTCAATGTTGGCATGCGAGGTACATCGAGAATCCGAGGGAACGCGC | 1300 |
| Qy | 401 | AspPheValGlySerPheArgHisGlyThrMetAlaAsnAlaLeuProHisAlaIleGly | 420 |
| Db | 1301 | GACTTTGTGGGTTCATCCGCCACGGCACGATGGCTAATGCGTTGCCTCATGCGATTGGT | 1360 |
| Qy | 421 | AlaGlnSerValAspArgAsnArgGlnValIleAlaMetCysGlyAspGlyGlyLeuGly | 440 |
| Db | 1361 | GCGCAAAGTGGATCGAAACGCCAGGTGATCGCGATGTGTCGAGTGGTTGGC | 1420 |
| Qy | 441 | MetLeuLeuGlyGluLeuLeuThrValLysLeuHisGlnLeuProLeuLysAlaValVal | 460 |
| Db | 1421 | ATGCTGCTGGGTGAGCTCTGACCGTTAAGCTGCACCAACTCCGCTGAAGGCTGTGGT | 1480 |
| Qy | 461 | PheAsnAsnSerSerLeuGlyMetValLysLeuGluMetLeuValGluGlyGlnProGlu | 480 |
| Db | 1481 | TTAACACAGTTCTTGGCATGGTAAGTTGGAGATGCTCGTGGAGGGACAGCCAGAA | 1540 |
| Qy | 481 | PheGlyThrAspHisGluGluValAsnPheAlaGluIleAlaAlaAlaGlyIleLys | 500 |
| Db | 1541 | TTGGTACTGACCATGAGGAAGTGAATTTCGAGAGATTGGCGGCTGGGGTATCAA | 1600 |
| Qy | 501 | SerValArgIleThrAspProLysLysValArgGluGlnLeuAlaGluAlaLeuAlaTyr | 520 |
| Db | 1601 | TCGGTACGCATCACCGATCCGAAGAAAGTTCGCAGCAGCTAGCTGAGGCATTGGCATAT | 1660 |
| Qy | 521 | ProGlyProValLeuIleAspIleValThrAspProAsnAlaLeuSerIleProProThr | 540 |
| Db | 1661 | CCTGGACCTGACTGATCGATATCGTCACGGATCTAATGCGCTGCGATCCCACCAACC | 1720 |
| Qy | 541 | IleThrTrpGluGlnValMetGlyPheSerLysAlaAlaThrArgThrValPheGlyGly | 560 |
| Db | 1721 | ATCACGTGGGAAACAGGTCACTGGATTCAAGCAAGGCGGCCACCGAACCGTCTTGGTGG | 1780 |
| Qy | 561 | GlyValGlyAlaMetIleAspLeuAlaArgSerAsnIleArgAsnIleProThrPro | 579 |
| Db | 1781 | GGAGTAGGAGCGATGATCGATCTGGCCCGTTCAACATAAGGAATATTCCACTCCA | 1837 |

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APPENDIX B

RESULT 1

us-10-781-014-85

Query Match 86.1%; Score 1860; DB 1; Length 1860;
 Best Local Similarity 100.0%; Pred. No. 0;
 Matches 1860; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 227 CTGGCAGGGGGCGAAGCGTGGCAACAACCTGGAATTAAAGAGCACAATTGAAGTCGCACC 286
 |||||||
 Db 1 CTGGCAGGGGGCGAAGCGTGGCAACAACCTGGAATTAAAGAGCACAATTGAAGTCGCACC 60

Qy 287 AAGTTAGGCAACACAATAGCCATAACGTTGAGGAGTTAGATGGCACACAGCTACGCAGA 346
 |||||||
 Db 61 AAGTTAGGCAACACAATAGCCATAACGTTGAGGAGTTAGATGGCACACAGCTACGCAGA 120

Qy 347 ACAATTAAATTGACACTTGGAAAGGCTCAAGGTGTGAAGCGAATTATGGTTGGTGGGTGA 406
 |||||||
 Db 121 ACAATTAAATTGACACTTGGAAAGGCTCAAGGTGTGAAGCGAATTATGGTTGGTGGGTGA 180

Qy 407 CAGCCTTAATCCGATCGTGGATGCTCTCGCCAACTCAGATATTGAGTGGGTGACGTTCG 466
 |||||||
 Db 181 CAGCCTTAATCCGATCGTGGATGCTCTCGCCAACTCAGATATTGAGTGGGTGACGTTCG 240

Qy 467 AAATGAGGAAGCGGGCGGCTTGCAGCCGGTGCAGGAAATCGTGTACTGGGGAGCTGGC 526
 |||||||
 Db 241 AAATGAGGAAGCGGGCGGCTTGCAGCCGGTGCAGGAAATCGTGTACTGGGGAGCTGGC 300

Qy 527 AGTATGTGCTGCTTCTTGTGGCTTGAAACACACACCTGATTCAAGGGCTTTATGATTG 586
 |||||||
 Db 301 AGTATGTGCTGCTTCTTGTGGCTTGAAACACACACCTGATTCAAGGGCTTTATGATTG 360

Qy 587 GCATCGAAATGGTGCAGGGTGTGGCCATCGCTAGCCATATTCCGAGTGCCCAGATTGG 646
 |||||||
 Db 361 GCATCGAAATGGTGCAGGGTGTGGCCATCGCTAGCCATATTCCGAGTGCCCAGATTGG 420

Qy 647 TTGACGTTCTCCAGGAAACGCATCCGGAGATTGTTAAAGGAATGCTCTGGTTACTG 706
 |||||||
 Db 421 TTGACGTTCTCCAGGAAACGCATCCGGAGATTGTTAAAGGAATGCTCTGGTTACTG 480

Qy 707 CGAGATGGTGAATGGTGGTGAGCAGGGTGAACGCATTTGCATCACCGGATTCCAC 766
 |||||||
 Db 481 CGAGATGGTGAATGGTGGTGAGCAGGGTGAACGCATTTGCATCACCGGATTCCAC 540

Qy 767 CATGGCGGGTAAAGGTGTGCGGTAGTGATTCTGGTGTATCGCTAAGGAAGACGC 826
 |||||||
 Db 541 CATGGCGGGTAAAGGTGTGCGGTAGTGATTCTGGTGTATCGCTAAGGAAGACGC 600

Qy 827 AGGTGACGGTACTTATTCCAATTCACTATTCTCTGGCACTCCTGTGGTGTCCCGGA 886
 |||||||
 Db 601 AGGTGACGGTACTTATTCCAATTCACTATTCTCTGGCACTCCTGTGGTGTCCCGGA 660

Qy 887 TCCTACTGAGGCTGCAGCGCTGGTGGAGGCAGTAAACACGCTAAGTCTGTCACCTTGT 946
 |||||||
 Db 661 TCCTACTGAGGCTGCAGCGCTGGTGGAGGCAGTAAACACGCTAAGTCTGTCACCTTGT 720

Qy 947 CTGGCGGTGCGGGCGTGAAGAATGCTCGCGCGCAGGTGTTGGAGTGGCGGAGAAGATTAA 1006
 |||||||
 Db 721 CTGGCGGTGCGGGCGTGAAGAATGCTCGCGCGCAGGTGTTGGAGTGGCGGAGAAGATTAA 780

Qy 1007 ATCACCGATCGGGCATCGCGCTGGTGGTAAGCAGTACATCCAGCATGAGAATCCGTTGA 1066
 |||||||
 Db 781 ATCACCGATCGGGCATCGCGCTGGTGGTAAGCAGTACATCCAGCATGAGAATCCGTTGA 840

Qy 1067 GGTCGGCATGTCGGCTGGCTGGTACGGCGCCTGCGTGGATGGCGTCAATGAGGCGGA 1126
 |||||||
 Db 841 GGTCGGCATGTCGGCTGGCTGGTACGGCGCCTGCGTGGATGGCGTCAATGAGGCGGA 900

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| | | | |
|----|------|--|------|
| Qy | 1127 | TCTGCTGATTCTATTGGGTACGGATTCCCTTATTCTGATTCCTCCTAAAGACAACGT | 1186 |
| Db | 901 | TCTGCTGATTCTATTGGGTACGGATTCCCTTATTCTGATTCCTCCTAAAGACAACGT | 960 |
| Qy | 1187 | TGCCAGGTGGATATCAACGGTGCACATTGGTCACGTACCAACGGTGAAGTATCCGT | 1246 |
| Db | 961 | TGCCAGGTGGATATCAACGGTGCACATTGGTCACGTACCAACGGTGAAGTATCCGT | 1020 |
| Qy | 1247 | GACCGGTGATGTTGCTGCAACAATCGAAAATATTTGCCCATGTGAAGGAAAAACAGA | 1306 |
| Db | 1021 | GACCGGTGATGTTGCTGCAACAATCGAAAATATTTGCCCATGTGAAGGAAAAACAGA | 1080 |
| Qy | 1307 | TCGTTCCCTCCTGATCGGATGCTCAAGGCACACGAGCGTAAGTTGACCTCGGTGGTAGA | 1366 |
| Db | 1081 | TCGTTCCCTCCTGATCGGATGCTCAAGGCACACGAGCGTAAGTTGACCTCGGTGGTAGA | 1140 |
| Qy | 1367 | GACGTACACACATAACGTCGAGAAGCATGTGCCTATTCAACCTGAATACGTTGCCCTAT | 1426 |
| Db | 1141 | GACGTACACACATAACGTCGAGAAGCATGTGCCTATTCAACCTGAATACGTTGCCCTAT | 1200 |
| Qy | 1427 | TTTGAACGAGCTGGCGATAAGGATGCGGTGTTACTGTGGATAACCGCATGTGCAATGT | 1486 |
| Db | 1201 | TTTGAACGAGCTGGCGATAAGGATGCGGTGTTACTGTGGATAACCGCATGTGCAATGT | 1260 |
| Qy | 1487 | GTGGCATGCGAGGTACATCGAGAATCGGAGGGACCGCGACTTGTGGGTTCAATTCCG | 1546 |
| Db | 1261 | GTGGCATGCGAGGTACATCGAGAATCGGAGGGACCGCGACTTGTGGGTTCAATTCCG | 1320 |
| Qy | 1547 | CCACGGCACGATGGCTAATCGTTGCCCATGCGATTGGTGCACAAAGTGTGATCGAAA | 1606 |
| Db | 1321 | CCACGGCACGATGGCTAATCGTTGCCCATGCGATTGGTGCACAAAGTGTGATCGAAA | 1380 |
| Qy | 1607 | CCGCCAGGTGATCGCGATGTGTGGCGATGGTGGTTGGCATGCTGCTGGTGAGCTTCT | 1666 |
| Db | 1381 | CCGCCAGGTGATCGCGATGTGTGGCGATGGTGGTTGGCATGCTGCTGGTGAGCTTCT | 1440 |
| Qy | 1667 | GACCGTTAAGCTGCACCAACTTCCGCTGAAGGCTGTGGTTAACACAGTTTTGGG | 1726 |
| Db | 1441 | GACCGTTAAGCTGCACCAACTTCCGCTGAAGGCTGTGGTTAACACAGTTTTGGG | 1500 |
| Qy | 1727 | CATGGTGAAGTGGAGATGCTCGTGGAGGGACAGCCAGAACATTGGTACTGACCATGAGGA | 1786 |
| Db | 1501 | CATGGTGAAGTGGAGATGCTCGTGGAGGGACAGCCAGAACATTGGTACTGACCATGAGGA | 1560 |
| Qy | 1787 | AGTGAATTCCGAGAGATTGGCGGGCTGGGTATCAAATCGTACGCATACCGATCC | 1846 |
| Db | 1561 | AGTGAATTCCGAGAGATTGGCGGGCTGGGTATCAAATCGTACGCATACCGATCC | 1620 |
| Qy | 1847 | GAAGAAAGTTCGCGAGCAGCTAGCTGAGGCATTGGCATATCCTGGACCTGTACTGATCGA | 1906 |
| Db | 1621 | GAAGAAAGTTCGCGAGCAGCTAGCTGAGGCATTGGCATATCCTGGACCTGTACTGATCGA | 1680 |
| Qy | 1907 | TATCGTCACGGATCTAATCGCTGTGATCCCACCAACCATCACGTGGAACAGGTAT | 1966 |
| Db | 1681 | TATCGTCACGGATCTAATCGCTGTGATCCCACCAACCATCACGTGGAACAGGTAT | 1740 |
| Qy | 1967 | GGGATTCAAGCAAGGCGGCCACCGAACCGTCTTGGTGGAGGAGTAGGAGCGATCGA | 2026 |
| Db | 1741 | GGGATTCAAGCAAGGCGGCCACCGAACCGTCTTGGTGGAGGAGTAGGAGCGATCGA | 1800 |
| Qy | 2027 | TCTGGCCCGTTCGAACATAAGGAATATTCCTACTCCATGATGATTGATACACCTGCTGTT | 2086 |
| Db | 1801 | TCTGGCCCGTTCGAACATAAGGAATATTCCTACTCCATGATGATTGATACACCTGCTGTT | 1860 |

Art Unit: 1652

APPENDIX CRESULT 1
us-09-456-306-1

Query Match 100.0%; Score 875; DB 1; Length 2160;
 Best Local Similarity 100.0%; Pred. No. 0;
 Matches 875; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 TCGAGATGGTGAATGGTGGTGGAGCAGGGTGAACGCATTTGCATCACCGATTCACTCC 60
 |||||||
 Db 705 TCGAGATGGTGAATGGTGGTGGAGCAGGGTGAACGCATTTGCATCACCGATTCACTCC 764
 |||||||
 Qy 61 ACCATGGCGGGTAAAGGTGTGCGGTGGTAGTGATTCTCTGGTATATCGCTAAGGAAGAC 120
 |||||||
 Db 765 ACCATGGCGGGTAAAGGTGTGCGGTGGTAGTGATTCTCTGGTATATCGCTAAGGAAGAC 824
 |||||||
 Qy 121 GCAGGTGACGGTACTTATTCCAATTCACTATTCTCTGGACTCCTGTGGTGTTC 180
 |||||||
 Db 825 GCAGGTGACGGTACTTATTCCAATTCACTATTCTCTGGACTCCTGTGGTGTTC 884
 |||||||
 Qy 181 GATCCTACTGAGGCTGCAGCGCTGGTGAGGGATTAAACAACGCTAAGTCTGTCACTTTG 240
 |||||||
 Db 885 GATCCTACTGAGGCTGCAGCGCTGGTGAGGGATTAAACAACGCTAAGTCTGTCACTTTG 944
 |||||||
 Qy 241 TTCTGCGGTGCGGGCGTGAAGAATGCTCGCGCAGGTGGAGTTGGAGGGAGAAGATT 300
 |||||||
 Db 945 TTCTGCGGTGCGGGCGTGAAGAATGCTCGCGCAGGTGGAGTTGGAGGGAGAAGATT 1004
 |||||||
 Qy 301 AAATCACCGATCGGGCATCGCCTGGTGGTAAGCAGTACATCCAGCATGAGAATCCGTTT 360
 |||||||
 Db 1005 AAATCACCGATCGGGCATCGCCTGGTGGTAAGCAGTACATCCAGCATGAGAATCCGTTT 1064
 |||||||
 Qy 361 GAGGTGGCATGTCCTGGCCTGCTGGTTACGGCGCTGCGTGGATCGTCCAATGAGGG 420
 |||||||
 Db 1065 GAGGTGGCATGTCCTGGCCTGCTGGTTACGGCGCTGCGTGGATCGTCCAATGAGGG 1124
 |||||||
 Qy 421 GATCTGCTGATTCTATTGGGTACGGATTCCCTTATTCTGATTTCTCTAAAGACAAC 480
 |||||||
 Db 1125 GATCTGCTGATTCTATTGGGTACGGATTCCCTTATTCTGATTTCTCTAAAGACAAC 1184
 |||||||
 Qy 481 GTTGCCTCAGGTGGATATCAACGGTGCACATTGGTCACGTACCGTGAAGTATCCG 540
 |||||||
 Db 1185 GTTGCCTCAGGTGGATATCAACGGTGCACATTGGTCACGTACCGTGAAGTATCCG 1244
 |||||||
 Qy 541 GTGACCGGTGATGTTGTCGAACAATCGAAAATATTTCCTCATGTAAGGAAAAAAC 600
 |||||||
 Db 1245 GTGACCGGTGATGTTGTCGAACAATCGAAAATATTTCCTCATGTAAGGAAAAAAC 1304
 |||||||
 Qy 601 GATCGTTCTTCTTGATCGATGCTCAAGGCACACGAGCGTAAGTTGAGCTCGTGGTA 660
 |||||||
 Db 1305 GATCGTTCTTCTTGATCGATGCTCAAGGCACACGAGCGTAAGTTGAGCTCGTGGTA 1364
 |||||||
 Qy 661 GAGACGTACACACATAACGTCGAGAAGCATGTGCCTATTACCGCTGAATACGTTGCCTCT 720
 |||||||
 Db 1365 GAGACGTACACACATAACGTCGAGAAGCATGTGCCTATTACCGCTGAATACGTTGCCTCT 1424
 |||||||
 Qy 721 ATTTGAACGAGCTGGCGATAAGGATGCGGTGTTACTGTGGATACGGCATGTGCAAT 780
 |||||||
 Db 1425 ATTTGAACGAGCTGGCGATAAGGATGCGGTGTTACTGTGGATACGGCATGTGCAAT 1484
 |||||||
 Qy 781 GTGTGGCATGCGAGGTACATCGAGAATCCGGAGGGACCGCGACTTGTGGGTTCAATT 840
 |||||||
 Db 1485 GTGTGGCATGCGAGGTACATCGAGAATCCGGAGGGACCGCGACTTGTGGGTTCAATT 1544
 |||||||
 Qy 841 CGCCACGGCACGATGGCTAATCGCTTGCCTCATGC 875
 |||||||
 Db 1545 CGCCACGGCACGATGGCTAATCGCTTGCCTCATGC 1579

Art Unit: 1652

APPENDIX DRESULT 1
us-09-456-306-3

Alignment Scores:

| | | | |
|------------------------|---------|---------------|-----|
| Pred. No.: | 0 | Length: | 875 |
| Score: | 1518.00 | Matches: | 291 |
| Percent Similarity: | 100.00% | Conservative: | 0 |
| Best Local Similarity: | 100.00% | Mismatches: | 0 |
| Query Match: | 50.85% | Indels: | 0 |
| DB: | 1 | Gaps: | 0 |

us-09-456-306-2 (1-579) x us-09-456-306-3 (1-875)

| | | |
|----|--|-----|
| Qy | 127 CysGluMetValAsnGlyGlyGluGlnGlyGluArgIleLeuHisHisAlaIleGlnSer | 146 |
| Db | 1 TCGCAGATGGTGAATGGTGGTAGCAGGGTAAACGCATTTCATCACGCGATTCAAGTCC | 60 |
| Qy | 147 ThrMetAlaGlyLysGlyValSerValValValIleProGlyAspIleAlaLysGluAsp | 166 |
| Db | 61 ACCATGGCGGGTAAAGGTGTGCGGTGGTAGTCATTCTGGTATATCGCTAAGGAAGAC | 120 |
| Qy | 167 AlaGlyAspGlyThrTyrSerAsnSerThrIleSerSerGlyThrProValValPhePro | 186 |
| Db | 121 GCAGGTGACGGTACTTATTCCAATTCCACTATTCCTCTGGCACTCCTGTGGTGTCCCG | 180 |
| Qy | 187 AspProThrGluAlaAlaAlaLeuValGluAlaIleAsnAsnAlaLysSerValThrLeu | 206 |
| Db | 181 GATCCTACTGAGGCTGCAGCGCTGGTGGAGGCATTAACACGCTAACGCTAACGTCTGTC | 240 |
| Qy | 207 PheCysGlyAlaGlyValLysAsnAlaArgAlaGlnValLeuGluLeuAlaGluLysIle | 226 |
| Db | 241 TTCTGCGGTGCGGGCGTGAAGAATGCTCGCGCAGGTGGAGTTGGCGGAGAACATT | 300 |
| Qy | 227 LysSerProIleGlyHisAlaLeuGlyGlyLysGlnTyrIleGlnHisGluAsnProPhe | 246 |
| Db | 301 AAATCACCGATCGGCATCGCCTGGTGGTAAGCAGTACATCCAGCATGAGAATCCGTTT | 360 |
| Qy | 247 GluValGlyMetSerGlyLeuLeuGlyTyrGlyAlaCysValAspAlaSerAsnGluAla | 266 |
| Db | 361 GAGGTGGCATGTCCTGGCTGCTTACGGCGCTGCGTGGATGCGTCCAATGAGGCG | 420 |
| Qy | 267 AspLeuLeuIleLeuLeuGlyThrAspPheProTyrSerAspPheLeuProLysAsn | 286 |
| Db | 421 GATCTGCTGATTCTATTGGGTACGGATTCCTTATTCTGATTCCCTAAAGACAAC | 480 |
| Qy | 287 ValAlaGlnValAspIleAsnGlyAlaHisIleGlyArgArgThrThrValLysTyrPro | 306 |
| Db | 481 GTTGGCCAGGTGGATATCAACGGTGCACATTGGTCGACGTACCAACGGTGAAGTATCCG | 540 |
| Qy | 307 ValThrGlyAspValAlaAlaThrIleGluAsnIleLeuProHisValLysGluLysThr | 326 |
| Db | 541 GTGACCGGTGATGTTGCTGCAACAAATCGAAAATTTGCCTCATGTGAAGGAAAAAACAA | 600 |
| Qy | 327 AspArgSerPheLeuAspArgMetLeuLysAlaHisGluArgLysLeuSerSerValVal | 346 |
| Db | 601 GATCGTTCCCTCCTGATGGATGCTCAAGGCACACGAGCGTAAGTTGAGCTCGGTGGTA | 660 |
| Qy | 347 GluThrTyrThrHisAsnValGluLysHisValProIleHisProGluTyrValAlaSer | 366 |
| Db | 661 GAGACGTACACACATAACGTCGAGAACATGTGCCTATTCAACCTGAATACGTTGCCTCT | 720 |
| Qy | 367 IleLeuAsnGluLeuAlaAspLysAspAlaValPheThrValAspThrGlyMetCysAsn | 386 |
| Db | 721 ATTTTGAACGAGCTGGCGATAAGGATGGGTGTTACTGTGGATACCGCATGTGCAAT | 780 |
| Qy | 387 ValTrpHisAlaArgTyrIleGluAsnProGluGlyThrArgAspPheValGlySerPhe | 406 |

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Db 781 |||||||GTGTGGCATGCGAGGTACATCGAGAATCCGAGGGAACGCGCGACTTGTGGGTTCATTC 840
Qy 407 ArgHisGlyThrMetAlaAsnAlaLeuProHis 417
Db 841 CGCACGGCACGATGGCTAATGCGTTGCCTCAT 873